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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOHN GAVIN MACDONALD and JASON LYE

Appeal 2010-000817
Application 10/731,256
Technology Center 1600

Decided: May 27, 2010

Before ERIC GRIMES, TONI R. SCHEINER, and STEPHEN WALSH, *Administrative Patent Judges*.

WALSH, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a method of administering a compound via nanoparticles. The Patent Examiner rejected the claims on the ground of obviousness. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

Claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 64 and 65 are on appeal.

Claim 28 is representative and reads as follows:

28. A method of using a triggerably releasable delivery system, the method comprising administering to a mucosal membrane of a patient a plurality of nanoparticles containing silica coated with alumina and having a size of about 500 nanometers or less, wherein the alumina provides a site on a surface of the nanoparticles to which is bonded a functional compound, wherein the nanoparticles possess a zeta potential of about 20 millivolts or more, wherein the nanoparticles are contained within a vehicle that further comprises a pH altering material, and wherein the functional compound is released from the surface of the nanoparticles upon exposure to a change in pH. (Emphasis added.)

The Examiner rejected the claims as follows:

- claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 64 and 65 under 35 U.S.C. § 103(a) over Bosch,[1] Breitbarth,[2] Ma[3] and Daraio[4]; and
- claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 64 and 65 under 35 U.S.C. § 103(a) over Tan,[5] Bosch, Breitbarth, Ma and Daraio.

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[1] William H. Bosch et al., *Nanoparticulate Compositions Comprising Inorganic Cores*, WO 03/032959, Apr. 24, 2003. The record contains two versions of the Bosch publication: the first, published Apr. 24, 2003; and a "Corrected Version" published May 13, 2004. We rely on and cite to the first, published Apr. 24, 2003.

[2] Richard Breitbarth, *Composition For Stimulating And Inducing Hair Growth*, U.S. Patent No. 5,597,575, issued Jan. 28, 1997.

[3] Yi Hua Ma et al., *Adsorption of Proteins and Antibiotics on Porous Alumina Membranes*, 80 FUNDAMENTALS OF ADSORPTION (MOTOYUKI SUZUKI ED. ELSEVIER pp. 389-396 (1993).

[4] Marta E. Daraio et al., *Aggregation and Photophysics of Rose Bengal in Alumina-Coated Colloidal Suspensions*, 84 HELVETICA CHIMICA ACTA 2601-2614 (2001).

Claims 30, 31, 33-35, 37, 38, 40, 42-44 and 64 have not been argued separately and therefore stand or fall with claim 28. 37 C.F.R. § 41.37(c)(1)(vii).

OBVIOUSNESS

The Issue

The Examiner's position is that "it would have been *prima facie* obvious for one skilled in the art at the time of the invention to apply the alumina coated silica nanoparticles with active agents adsorbed thereon to mucosal membranes, as taught by Bosch et al., with the expectation that a small change in pH will readily and controllably release the active agent from the surface of the nanoparticles, as reasonably taught by Breitbarth and Ma et al." (Ans. 7.)

Appellants contend that (1) the references "fail to teach or suggest nanoparticles contained within a vehicle that further comprises a pH altering material" (App. Br. 7); (2) "[t]he Examiner improperly combines the teachings of Bosch with Breitbarth" and Breitbarth teaches away from the claimed invention (*id.* at 8-9); and (3) claim 65 is patentable because although Ma teaches that the amount of tetracycline adsorbed is a function of pH, "it cannot be said that Ma obviates releasing tetracycline from the surface upon exposure to a change in pH" (*id.* at 10)

The issues with respect to this appeal are:

whether the references teach or suggest nanoparticles contained within a vehicle that further comprises a pH altering material;

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[5] Weihong Tan et al., *Coated Nanoparticles*, U.S. Patent No. 6,548,264 B1, issued Apr. 15, 2003.

whether Breitbarth taught away from the claimed invention; and

whether Ma taught or suggested that tetracycline would be released from alumina by a pH change.

Findings of Fact

1. Bosch taught pharmaceutical compositions comprising "at least one nanoparticulate inorganic core, at least one active agent [i.e., functional compound] adsorbed or bound to the surface of the core, and a pharmaceutically acceptable carrier [i.e., vehicle], as well as any desired excipients." (*Id.* at 5:15-19.)
2. Bosch taught that "[t]he active agent can be a drug," and listed a variety of drugs including antibiotics. (*Id.* at 11-13.)
3. We find that Appellants' "functional compound" corresponds to the "active agent" that Bosch taught.
4. Bosch taught that "liquid application forms include emulsions, suspensions, syrups, and elixirs." (*Id.* at 23:15.)
5. Appellants' Specification states: "[t]he particles can be used as is, for instance, or can be combined with a liquid, gel or other vehicle which may facilitate delivery of the particles depending on the particular application. Such liquid and gel vehicles are known to those skilled in the art." (Spec. 5, ll. 24-26.)
6. We find that Appellants' "vehicle" corresponds to the "carrier" that Bosch taught.
7. Bosch taught that useful nanoparticles were preferably within the size range that Appellants claim (*id.* at 10:15-26), and described a working example using Ludox CL®, a 12 nanometer alumina coated silica, as

the inorganic core, coated with the functional compound naproxen (*id.* at 29:4-10).

8. In a section titled "Active Agents Useful in Mucous Applications," Bosch taught applying the nanoparticles with active agent to mucosal membranes including orally, to the lungs, throat and gastrointestinal tract. (*Id.* at 14:11-20.)

9. According to Bosch, "[o]ther pharmaceutical therapeutic methodologies include colonic, oral, rectal, intravaginal, . . . , pulmonary, nasal, buccal, topical, local, . . . , buccal spray, or nasal spray administration." (*Id.* at 14:21-24.)

10. Bosch taught that "[p]harmaceutical compositions according to the invention may also comprise one or more . . . buffers . . . . Such excipients are known in the art." (*Id.* at 20:8-11.)

11. The Specification states: "triggering of the delivery system may be accomplished through . . . introducing chemistries such as pH altering materials to the delivery systems to trigger the release of functional compounds. Chemistries that may be introduced to a delivery system include bicarbonates, carbonates and buffering salts . . . ." (Spec. 16, ll. 4-10.)

12. We find that Appellants' "pH altering material" includes "buffering salts" and corresponds to the "buffer" that Bosch taught.

13. The Examiner found that Bosch's nanoparticles had the claimed zeta potential (Ans. 6), and Appellants state they "have not challenged this disclosure of Bosch" (Reply Br. 5).

14. According to Breitbarth, "[t]opical application for administering drugs and even for controlled release of drugs is now used extensively." (Breitbarth, col. 3, ll. 32-34.)

15. Ma stated: "[t]he equilibrium adsorption of . . . the antibiotic tetracycline on alumina membranes was measured as a function of pH." (*Id.* at 389, Introduction.)

16. Ma disclosed that tetracycline's equilibrium adsorption on alumina was a function of pH. (Ma 389 (Abstract, Introduction); 391 (Results and Discussion, Fig. 1); 392 (Fig. 2 and Table 1).)

Principles of Law

When determining whether a claim is obvious, an Examiner must make "a searching comparison of the claimed invention – including all its limitations – with the teaching of the prior art." *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995). A prior art reference is said to teach away from an Applicant's invention "when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994). "Obviousness does not require absolute predictability of success. . . . [A]ll that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988).

Analysis

Claim 28

We agree with the Examiner's findings concerning the scope and content of Bosch, Breitbarth and Ma. While we agree with the Examiner that Bosch did not disclose that the active molecule would be released from the nanoparticle as a result of change in pH, we agree that a person of ordinary skill in the art, informed by Breitbarth and Ma, would have expected a change in pH to readily release the active agent from Bosch's nanoparticles. We find the Bosch, Breitbarth and Ma disclosures sufficient evidence to conclude that the subject matter claimed would have been obvious. The Examiner has not shown how the Tan and Daraio disclosures add substantially to the prima facie case of obviousness, nor have Appellants persuaded us that either reference weakens it. Under these circumstances, we find it unnecessary to discuss Tan or Daraio further.

Contrary to Appellants' first argument (*see* App. Br. 7), we find that Bosch taught nanoparticles contained within a vehicle that further comprises a pH altering material. We also find that Breitbarth's disclosure, that topical application of controlled release drugs was common, did not teach away from the claimed invention. Appellants offer no evidence that a person of ordinary skill in the art would have doubted Breitbarth's statement merely because it was made in the context of an invention for hair treatment. Nor do we find that Breitbarth would have discouraged a person of ordinary skill in the art from applying Bosch's method. Thus, we find Appellants' "teaching away" argument unpersuasive. (*See* App. Br. 8-9.)

Claim 65

Claim 65 is directed to the method of claim 28, through claim 64, "wherein the functional compound includes tetracycline." Appellants contend that Ma concerned only the conditions under which tetracycline could be adsorbed to alumina, and did not teach or suggest that tetracycline would be released from alumina by a pH change. (App. Br. 10.) Thus, Ma could not have supported an expectation of success for using tetracycline as Bosch's antibiotic. We disagree. Ma described the adsorption of tetracycline to alumina as a pH dependent "equilibrium adsorption." Ma showed that at some pH values, equilibrium favored adsorption, and at other pH values equilibrium did not favor adsorption, i.e., adsorbed tetracycline would desorb. We find this evidence supports the Examiner's findings that (1) tetracycline would be released from alumina by a pH change, and (2) there would have been a reasonable expectation of success in using tetracycline as the antibiotic in Bosch's method.

CONCLUSIONS

Bosch taught nanoparticles contained within a vehicle that further comprised a pH altering material.

Breitbarth did not teach away from the claimed invention.

Ma taught or suggested that tetracycline would be released from alumina by a pH change.

SUMMARY

We affirm the rejection of claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 64 and 65 under 35 U.S.C. § 103(a) over Bosch, Breitbarth, Ma and Daraio; and

We affirm the rejection of claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 64 and 65 under 35 U.S.C. § 103(a) over Tan, Bosch, Breitbarth, Ma and Daraio.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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